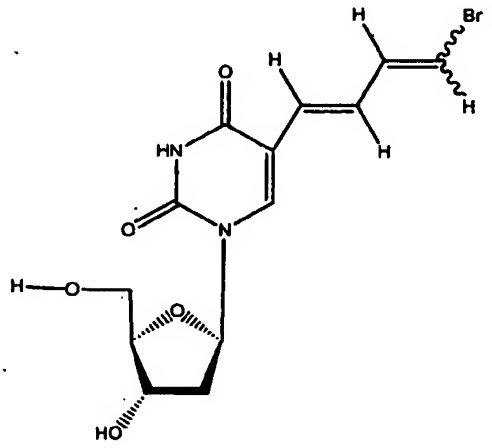
AMENDMENTS

In the claims:

Please cancel claims 1-52, without prejudice or disclaimer.

Please add the following new claims:

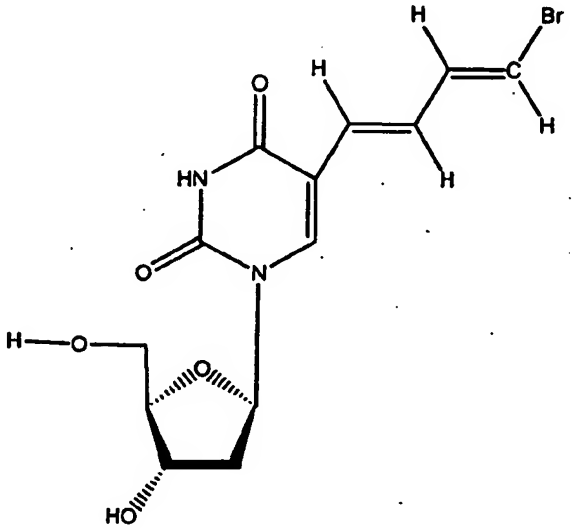
53. (New) A compound having the structure:



and its pharmaceutically acceptable salt.

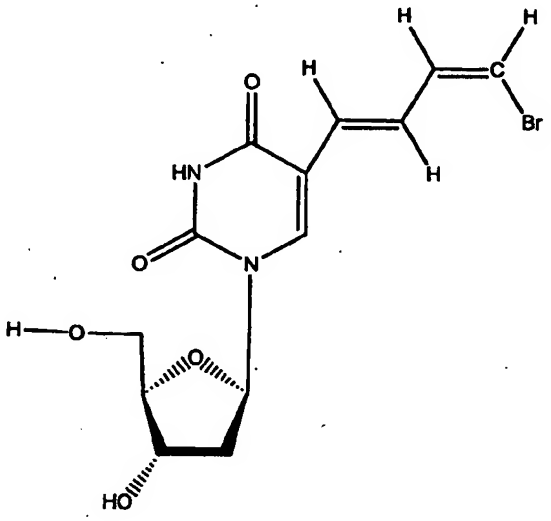
54. (New) The compound of claim 53, wherein the compound is comprised of a mixture of the E and Z isomers.

55. (New) The compound of claim 54, wherein the compound is the E isomer having the structure:



and its pharmaceutically acceptable salt.

56. (New) The compound of claim 54, wherein the compound is the Z isomer having the structure:



and its pharmaceutically acceptable salt.

57. (New) A composition comprising the compound of any of claims 53 to 56 and a carrier.

58. (New) A composition according to claim 57, wherein the carrier is a pharmaceutically acceptable carrier.

59. (New) A method for inhibiting the proliferation of a pathological cell *in vitro*, wherein thymidylate synthase is overexpressed in the cell, comprising contacting the cell with an effective amount of the compound according to any of claims 53 to 56.

60. (New) A method according to claim 59, wherein the pathological cell is a colon cancer cell, a breast cancer cell, a gastric cancer cell, a head and neck cancer cell, a liver cancer cell, or a pancreatic cancer cell.

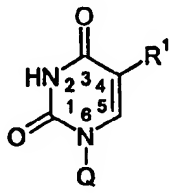
61. (New) A method according to claim 59, wherein the pathological cell is a colon cancer cell.

62. (New) Use of the compound according to any of claims 53 to 56 for the manufacture of a medicament for use in the treatment of a pathology characterized by pathological cells that overexpress thymidylate synthase.

In the Claims:

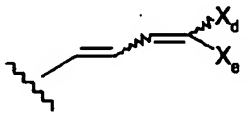
Please cancel claims 2 to 52 without prejudice or disclaimer. Please add new claims 53 to 83, as follows:

63 ~~53~~. (NEW) A compound or a pharmaceutically acceptable salt of the compound, wherein the compound has the structure:



wherein:

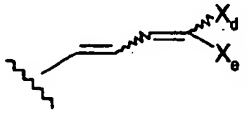
(i) R^1 is a group:



wherein X_d is H; and, X_e is Cl or Br;

or:

(ii) R^1 is a group:



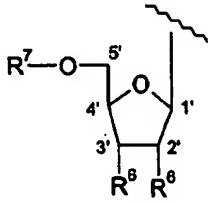
wherein X_d and X_e are independently the same or different and are selected from Cl, Br, I, and CN; not made or tested

or:

(iii) R^1 is a group:

wherein Q is:

not equiv. chemically (pseudohalogen)



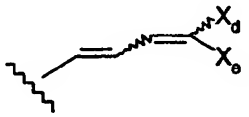
wherein each R^6 is independently -H, -OH, -OC(=O)CH_3, or -F; and,

R^7 is -H, a phosphate group, a phosphodiester group, or a phosphoramidate group;

wherein the compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, including D-form, L-form, α-anomeric form, and β-anomeric form.

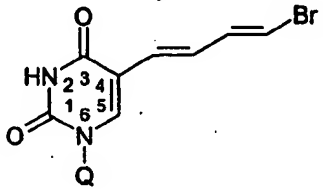
64 54. (NEW) A compound according to claim 53, wherein:

R^1 is a group:

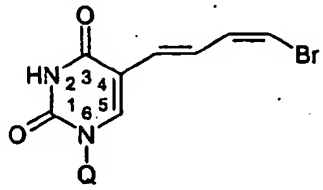


wherein X_d is H; and, X_e is Cl or Br.

65 55. (NEW) A compound according to claim 53, having the structure:

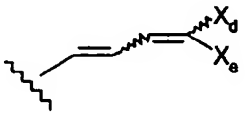


66 56. (NEW) A compound according to claim 53, having the structure:



67 57. (NEW) A compound according to claim 53, wherein:

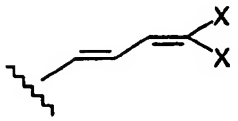
R^1 is a group:



wherein X_d and X_e are independently the same or different and are selected from Cl, Br, I, and CN.

68 ~~58.~~ (NEW) A compound according to claim ~~53~~ 63, wherein:

R^1 is a group:

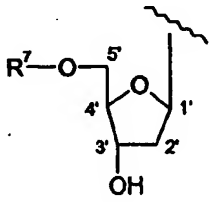


wherein each X is selected from Cl, Br, I, and CN.

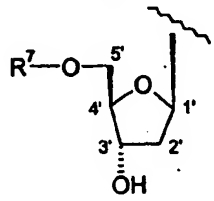
69 ~~59.~~ (NEW) A compound according to claim ~~58~~ 68, wherein X is Cl or Br.

70 ~~60.~~ (NEW) A compound according to claim ~~58~~ 68, wherein X is Br.

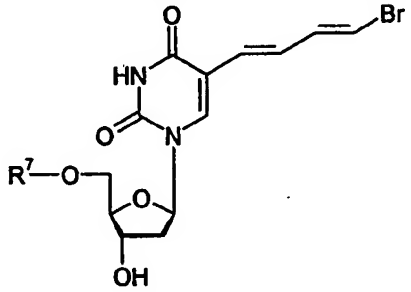
71 ~~61.~~ (NEW) A compound according to claim ~~53~~ 63, wherein Q is:



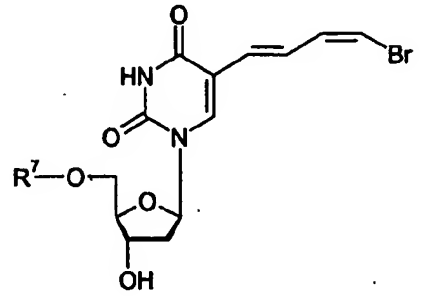
72 ~~62.~~ (NEW) A compound according to claim ~~53~~ 63, wherein Q is:



73 ~~63.~~ (NEW) A compound according to claim ~~53~~ 63, having the structure:



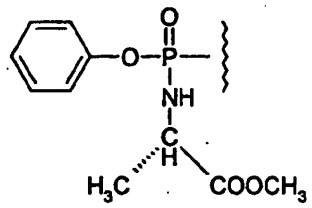
64. (NEW) A compound according to claim 63, having the structure:



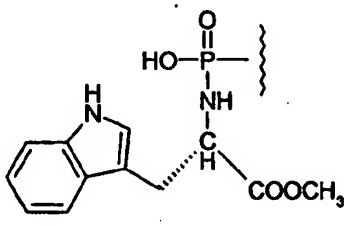
65. (NEW) A compound according to claim 63, wherein R^7 is -H.

66. (NEW) A compound according to claim 63, wherein R^7 is a phosphoramidate group derived from an amino acid.

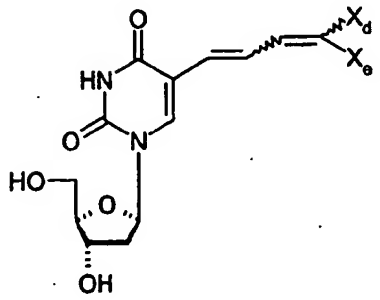
67. (NEW) A compound according to claim 63, wherein R^7 is:



68. (NEW) A compound according to claims 63, wherein R^7 is:

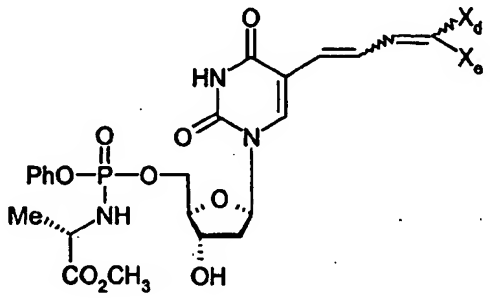


79 ~~69.~~ (NEW) A compound according to claim ~~53~~ 63, having the structure:



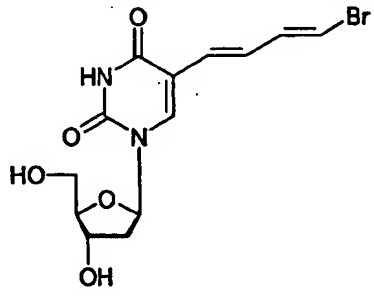
wherein X_d is H; and, X_e is Cl or Br.

80 ~~70.~~ (NEW) A compound according to claim ~~53~~ 63, having the structure:

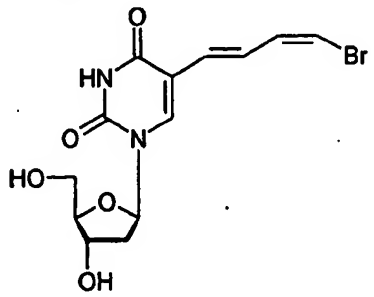


wherein X_d is H; and, X_e is Cl or Br.

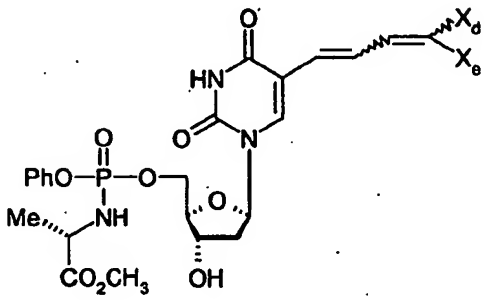
81 ~~71.~~ (NEW) A compound according to claim ~~53~~ 63, having the structure:



82 72. (NEW) A compound according to claim 63, having the structure:



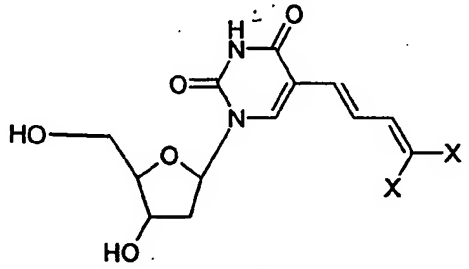
83 73. A compound according to claim 63, having the structure:



wherein X_d and X_e are independently the same or different and are selected from Cl, Br, I, and CN.

Not Posted

84 74. (NEW) A compound according to claim 63, having the structure:



wherein each X is selected from Cl, Br, I, and CN.

85 75. (NEW) A composition comprising a compound according to claim 63 and a carrier.

86 76. (NEW) A composition comprising a compound according to claim 63, and a pharmaceutically acceptable carrier.

87 ~~77.~~ (NEW) A method for screening for a therapeutic agent, comprising:

(a) contacting a sample containing a target cell with a compound according to claim ~~53~~ 63;

(b) contacting a separate sample of the target cell with a potential therapeutic agent; and

(c) comparing the samples for inhibition of cellular proliferation or cell killing.

88 ~~78.~~ (NEW) A method according to claim ~~77~~ 87, wherein the target cell is characterized as resistant to a chemotherapeutic drug.

89 ~~79.~~ (NEW) A method according to claim ~~77~~ 87, wherein the target cell is characterized as expressing a target enzyme that is amplified as a result of selection *in vivo* by chemotherapy.

90 ~~80.~~ (NEW) A method according to claim ~~77~~ 87, wherein the target enzyme is an endogenous intracellular enzyme that is overexpressed in the target cell.

91 ~~81.~~ (NEW) A method for inhibiting the proliferation of a pathological cell, wherein thymidylate synthase is overexpressed in the cell, comprising contacting the cell with an effective amount of the compound according to claim ~~53~~ 63.

92 ~~82.~~ (NEW) A method according to claim ~~81~~ 91, wherein the pathological cell is a colon cancer cell, a breast cancer cell, a gastric cancer cell, a head and neck cancer cell, a liver cancer cell, or a pancreatic cancer cell.

93 ~~83.~~ (NEW) A method according to claim ~~81~~ 91, wherein the pathological cell is a colon cancer cell.

I. AMENDMENTS

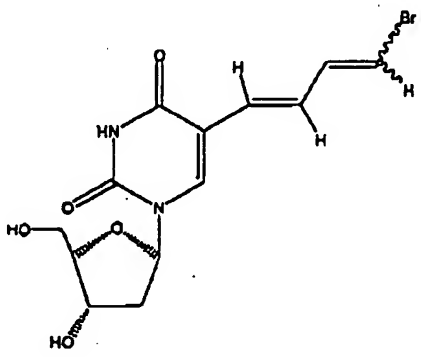
In the Claims:

The following Listing of the Claims replaces all prior versions, listings and amendments.

Listing of the Claims:

Claims 1. to 52. (Previously Canceled)

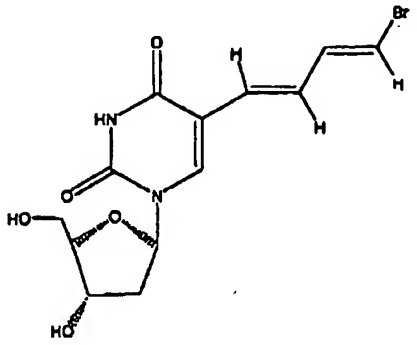
53. (Currently Amended) A compound having the structure:



and ~~its~~ pharmaceutically acceptable ~~salt~~ salts thereof.

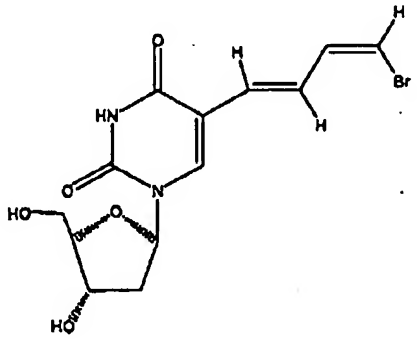
54. (Currently Amended) The compound of claim 53, wherein the compound is comprised of a mixture of the terminal halogenated double bond E and Z isomers.

55. (Currently Amended) The compound of claim 54, wherein the compound is the E isomer having the structure:



and ~~its~~ pharmaceutically acceptable ~~salt~~ salts thereof.

56. (Currently Amended) The compound of claim 54, wherein the compound is the Z isomer having the structure:



and ~~its~~ pharmaceutically acceptable ~~salt~~ salts thereof.

57. (Currently Amended) A composition comprising ~~the~~ a compound of any of claims 53 to 56 and a carrier.

58. (Currently Amended) A pharmaceutical composition according to claim 57, wherein the carrier is a pharmaceutically acceptable carrier.

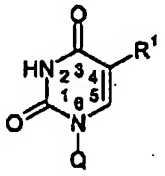
59. (Currently Amended) A method for inhibiting the proliferation of a pathological cell *in vitro*, wherein thymidylate synthase is overexpressed in the cell, comprising contacting the cell with an effective amount of ~~the~~ a compound according to any of claims 53 to 56.

60. (Previously Presented) A method according to claim 59, wherein the pathological cell is a colon cancer cell, a breast cancer cell, a gastric cancer cell, a head and neck cancer cell, a liver cancer cell, or a pancreatic cancer cell.

61. (Previously Presented) A method according to claim 59, wherein the pathological cell is a colon cancer cell.

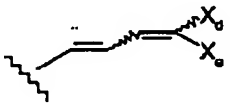
62. (Currently Canceled)

63. (Previously Presented) A compound or a pharmaceutically acceptable salt of the compound, wherein the compound has the structure:



wherein:

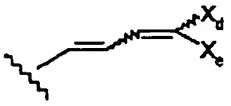
(i) R^1 is a group:



wherein X_d is H; and, X_e is Cl or Br;

or:

(ii) R^1 is a group:

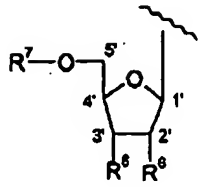


wherein X_d and X_e are independently the same or different and are selected from Cl, Br, I, and CN;

or:

(iii) R^1 is a group:

wherein Q is:



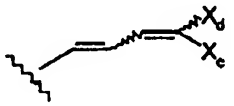
wherein each R^6 is independently -H, -OH, -OC(=O)CH_3, or F; and,

R^7 is -H, a phosphate group, a phosphodiester group, or a phosphoramidate group;

wherein the compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, including D-form, L-form, α-anomeric form, and β-anomeric form.

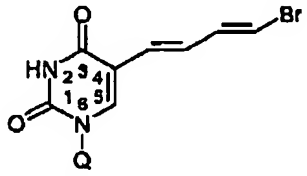
64. (Previously Presented) A compound according to claim 63, wherein:

R^1 is a group:

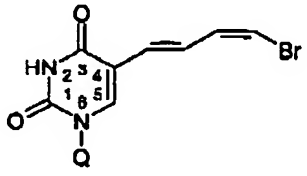


wherein X_d is H; and, X_e is Cl or Br.

65. (Currently Amended) A compound according to claim 63, having the structure:

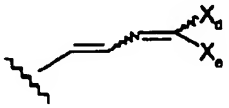


66. (Previously Presented) A compound according to claim 63, having the structure:



67. (Previously Presented) A compound according to claim 63, wherein:

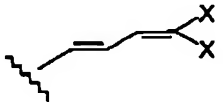
R^1 is a group:



wherein X_d and X_e are independently the same or different and are selected from Cl, Br, I, and CN.

68. (Previously Presented) A compound according to claim 63, wherein:

R^1 is a group:

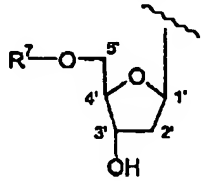


wherein each X is selected from Cl, Br, I, and CN.

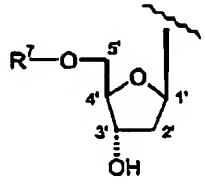
69. (Previously Presented) A compound according to claim 68, wherein X is Cl or Br.

70. (Previously Presented) A compound according to claim 68, wherein X is Br.

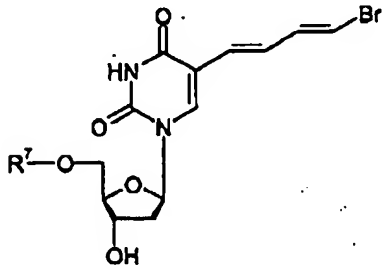
71. (Currently Amended) A compound according to claim 63, wherein Q is:



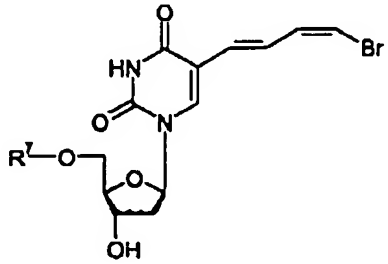
72. (Currently Amended) A compound according to claim 63, wherein Q is:



73. (Currently Amended) A compound according to claim 63, having the structure:



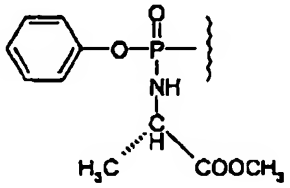
74. (Currently Amended) A compound according to claim 63, having the structure:



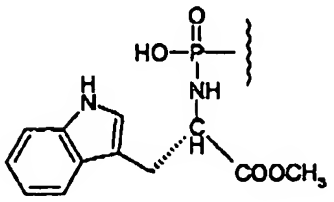
75. (Previously Presented) A compound according to claim 63, wherein R^7 is -H.

76. (Previously Presented) A compound according to claim 63, wherein R^7 is a phosphoramidate group derived from an amino acid.

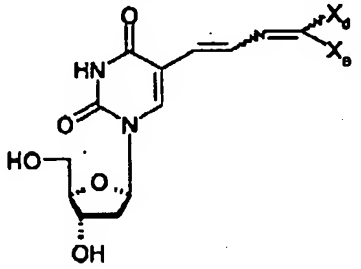
77. (Currently Amended) A compound according to claim 63, wherein R^7 is:



78. (Currently Amended) A compound according to claims 63, wherein R^7 is:

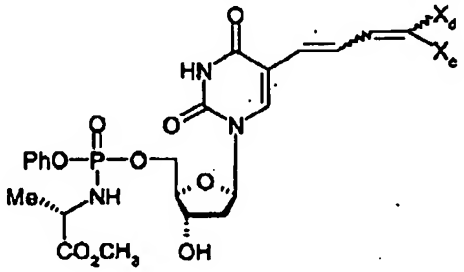


79. (Previously Presented) A compound according to claim 63, having the structure:



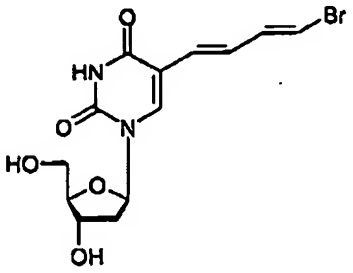
wherein X_d is H; and, X_e is Cl or Br.

80. (Currently Amended) A compound according to claim 63, having the structure:

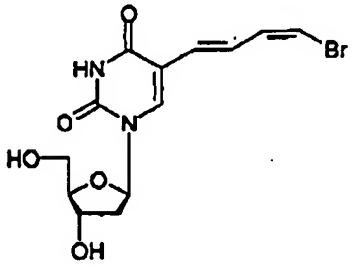


wherein X_d is H; and, X_e is Cl or Br.

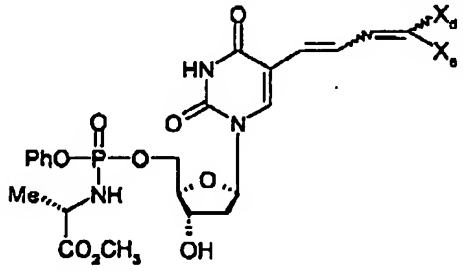
81. (Currently Amended) A compound according to claim 63, having the structure:



82. (Currently Amended) A compound according to claim 63, having the structure:

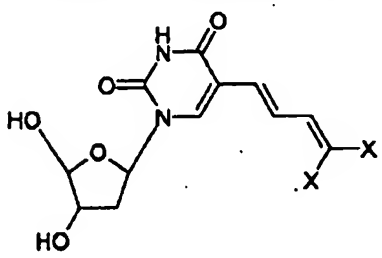


83. (Previously Presented) A compound according to claim 63, having the structure:



wherein X_d and X_e are independently the same or different and are selected from Cl, Br, I, and CN.

84. (Previously Presented) A compound according to claim 63, having the structure:



wherein each X is selected from Cl, Br, I, and CN.

85. (Previously Presented) A composition comprising a compound according to claim 63 and a carrier.

86. (Previously Presented) A composition comprising a compound according to claim 63, and a pharmaceutically acceptable carrier.

87. (Previously Presented) A method for screening for a therapeutic agent, comprising:

(a) contacting a sample containing a target cell with a compound according to claim 63;

(b) contacting a separate sample of the target cell with a potential therapeutic agent; and

(c) comparing the samples for inhibition of cellular proliferation or cell killing.

88. (Previously Presented) A method according to claim 86, wherein the target cell is characterized as resistant to a chemotherapeutic drug.

89. (Previously Presented) A method according to claim 86, wherein the target cell is characterized as expressing a target enzyme that is amplified as a result of selection *in vivo* by chemotherapy.

90. (Previously Presented) A method according to claim 86, wherein the target enzyme is an endogenous intracellular enzyme that is overexpressed in the target cell.

91. (Previously Presented) A method for inhibiting the proliferation of a pathological cell, wherein thymidylate synthase is overexpressed in the cell, comprising contacting the cell with an effective amount of the compound according to claim 63.

92. (Previously Presented) A method according to claim 90, wherein the pathological cell is a colon cancer cell, a breast cancer cell, a gastric cancer cell, a head and neck cancer cell, a liver cancer cell, or a pancreatic cancer cell.

93. (Previously Presented) A method according to claim 90, wherein the pathological cell is a colon cancer cell.

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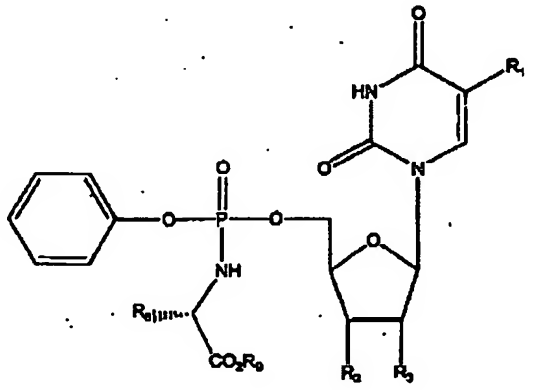
Amendments to the Claims

This listing of Claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound having the formula:



wherein R_1 is selected from the group consisting of alkyl, alkenyl, alkynyl, vinyl, propargyl and substituted derivatives thereof;

wherein R_2 and R_3 are independently the same or different and are selected from the group consisting of ~~Br, Cl, F, I~~, H, OH, $OC(=O)CH_3$, ~~-O-~~and -O-Rg, wherein Rg is a hydroxyl protecting group other than acetyl;

wherein R_8 is a side chain of any naturally occurring amino acid or an analogue of said side chain ~~of said naturally occurring amino acid~~;

and wherein R_9 is selected from the group consisting of hydrogen, an aliphatic group, an alicyclic group, an aromatic group ~~and~~ a heterocyclic group ~~and derivatives and~~ or, an adamantyl group ~~and analogs of R_9~~;

and any enantiomeric, diastereomeric, or stereoisomeric form, including D-form, L-form, α-anomeric form, and β-anomeric form, and its pharmaceutically acceptable salts~~, esters and ethers of these compounds~~.

2. (Previously Amended) The compound of claim 1, wherein R_8 is a side chain of an amino acid selected from the group consisting of alanine, glycine, tryptophan, leucine and aspartic acid.

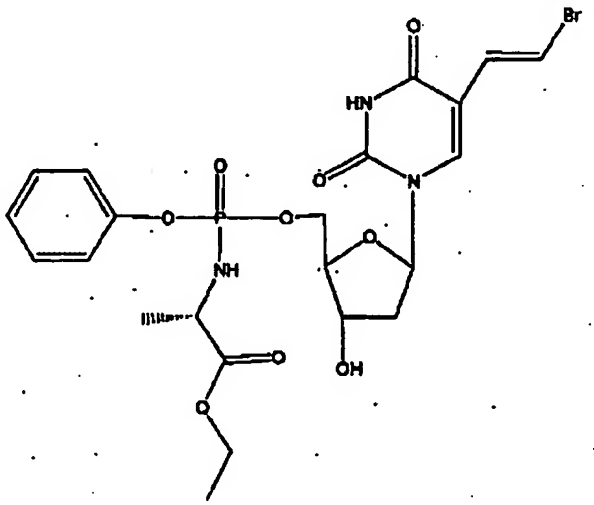
3. (Original) The compound of claim 1, wherein R_1 is a halogen-substituted vinyl derivative.

4. (Original) The compound of claim 3, wherein R_1 is bromovinyl.

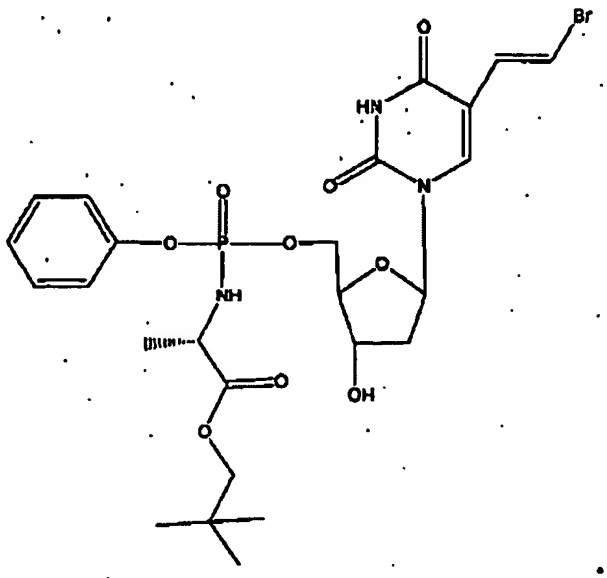
5. (Previously Amended) The compound of claim 4, wherein the amino acid is alanine and therefore R_8 is methyl, with the proviso that R_9 is not methyl.

6. (Previously Amended) The compound of claim 5, wherein R_9 is selected from the group consisting of -CH_2-phenyl, -CH_2-cyclopropyl, cyclohexyl, iso-propyl, -CH_2-*tert*-butyl, cycloheptyl, cyclooctyl and -CH_2-adamantyl.

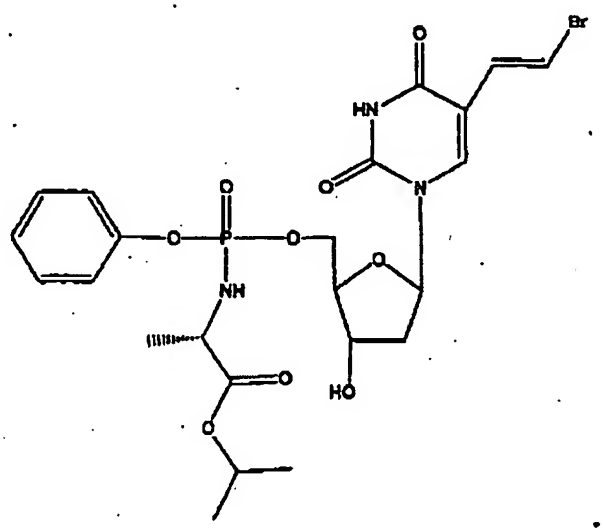
7. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



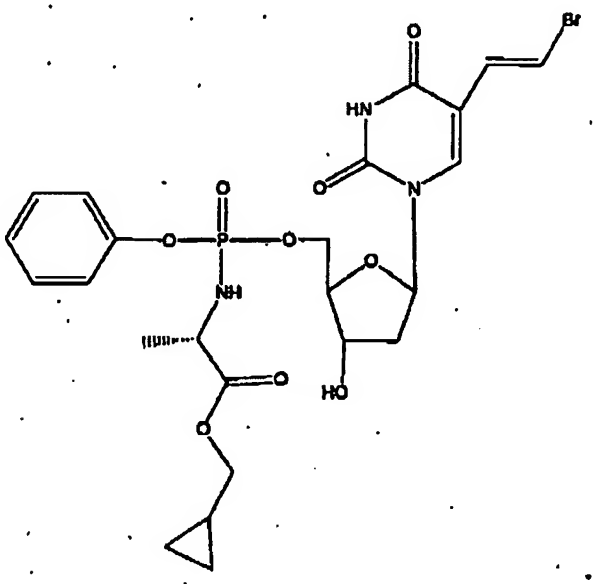
8. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



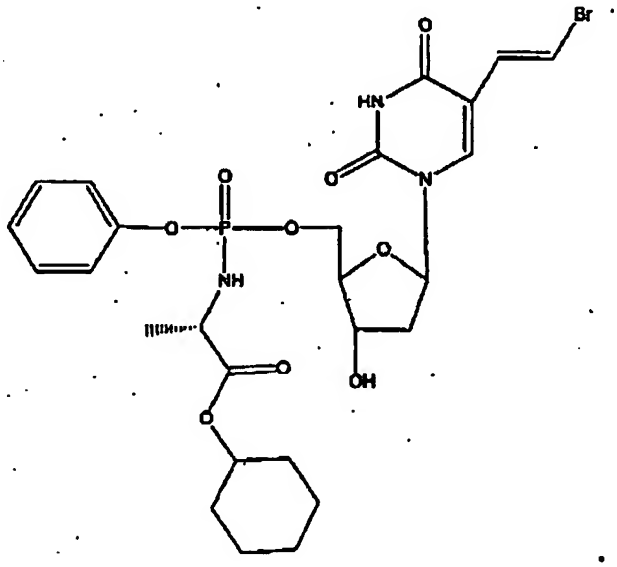
9. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



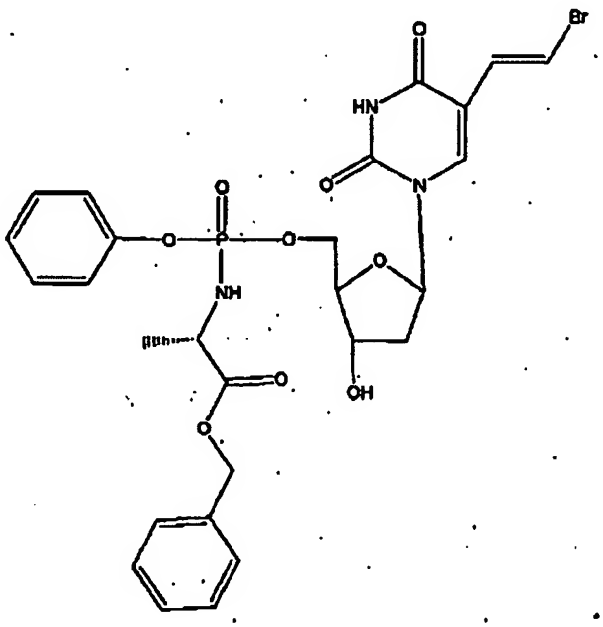
10. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



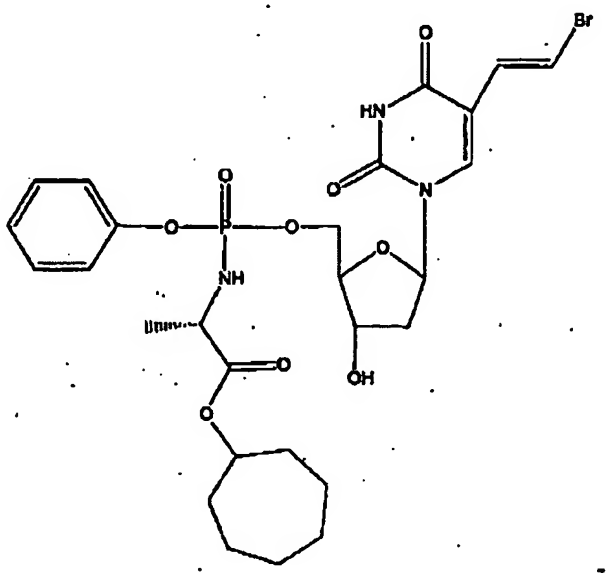
11. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



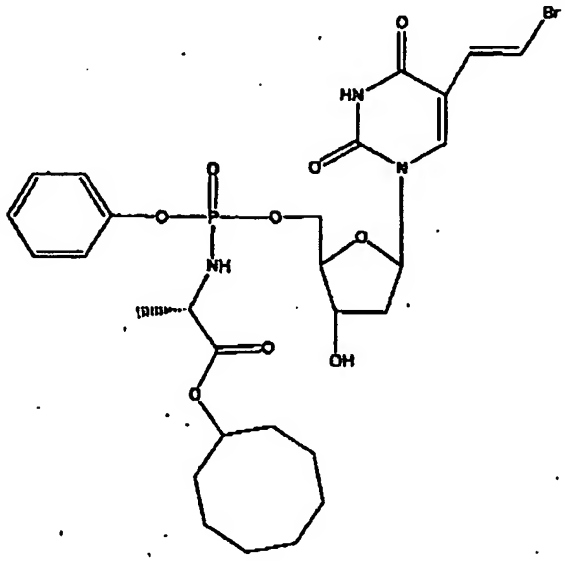
12. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



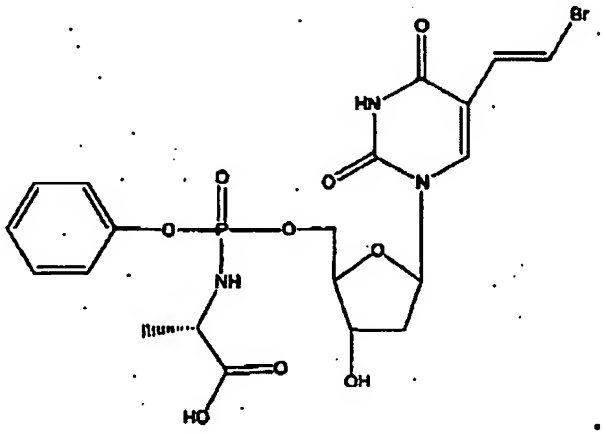
13. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



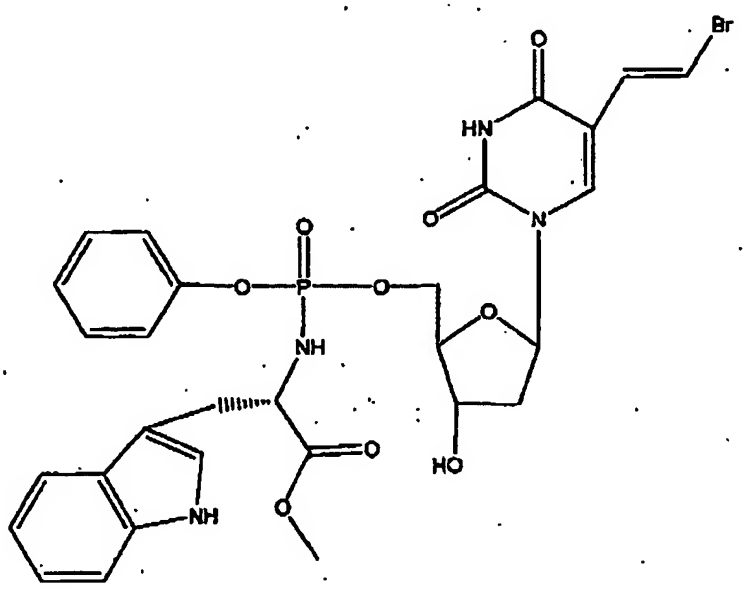
14. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:

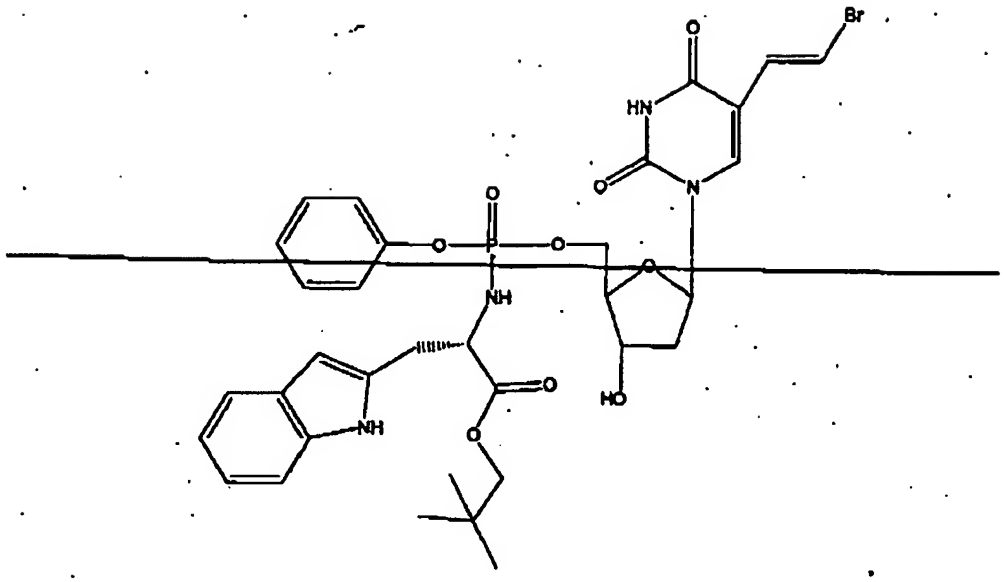


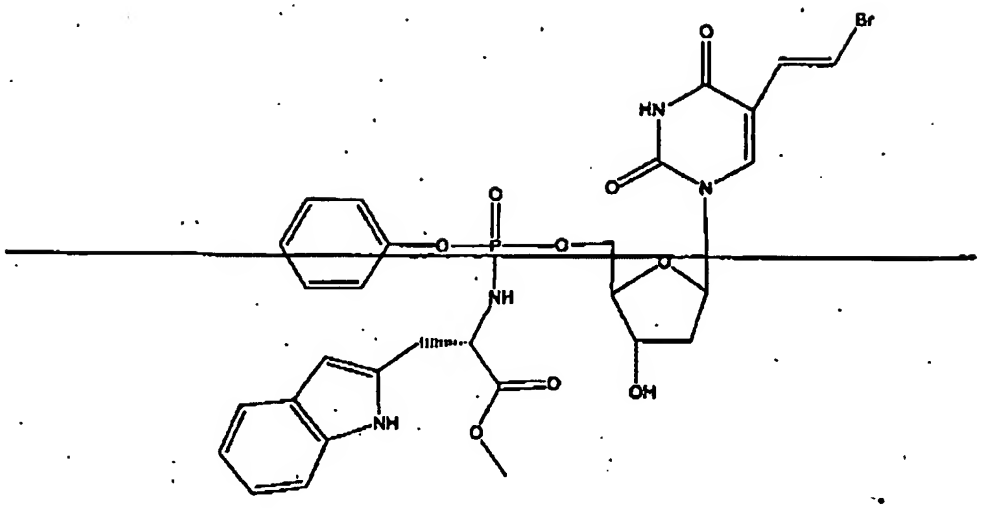
15. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



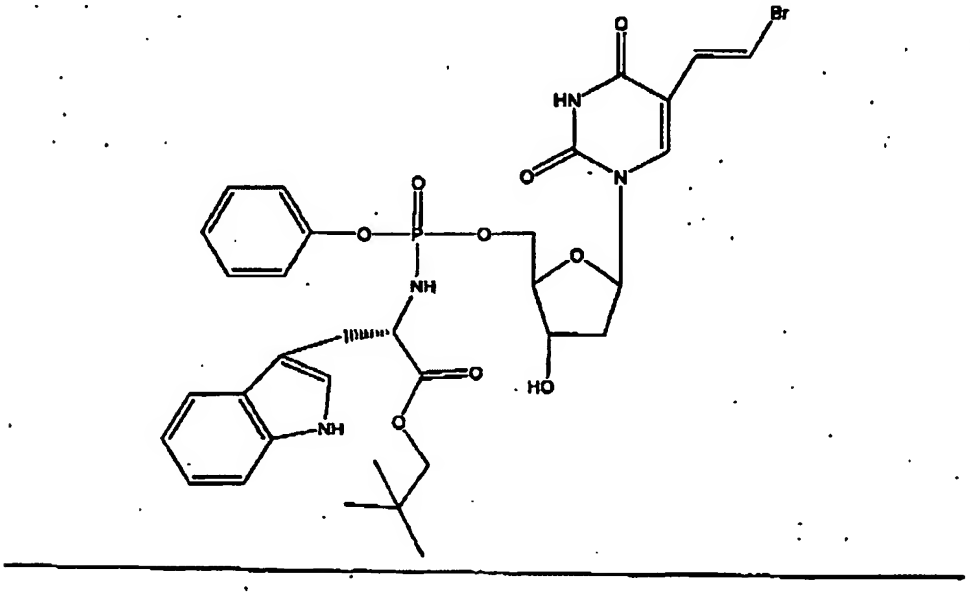
16. (Currently Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



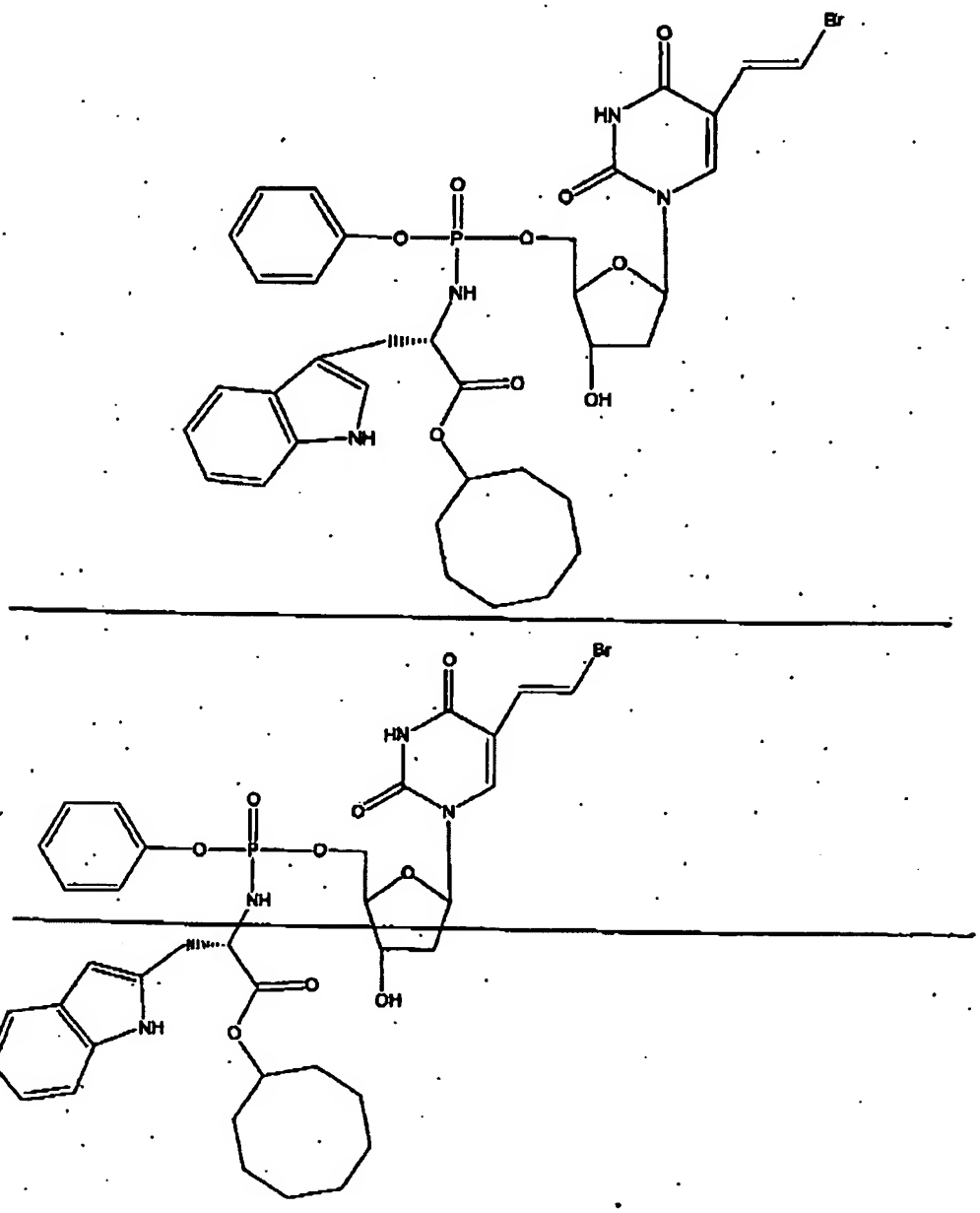




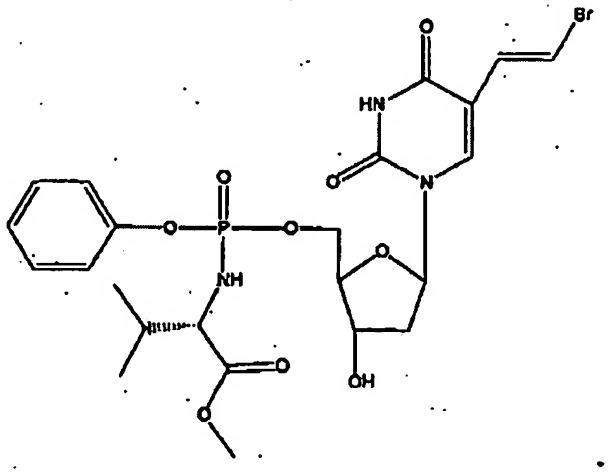
17. (Currently Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



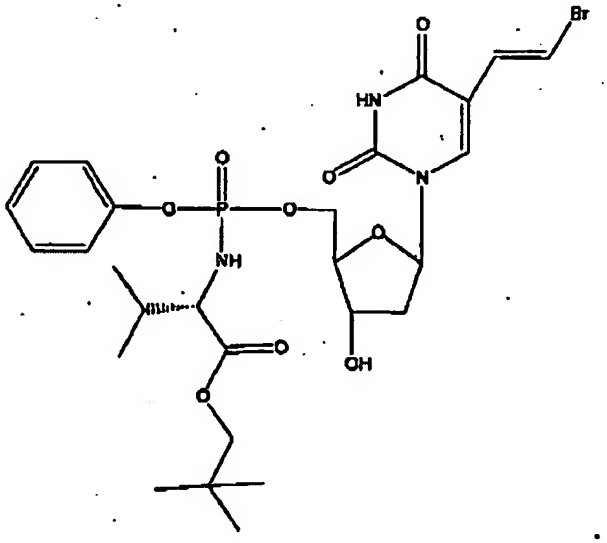
18. (Currently Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



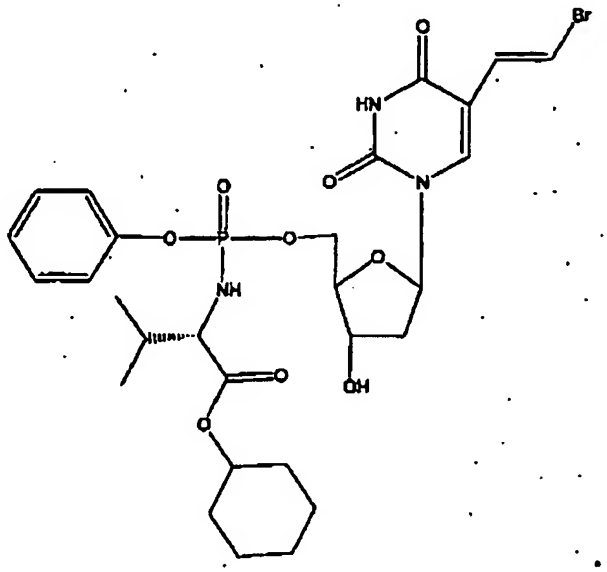
19. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



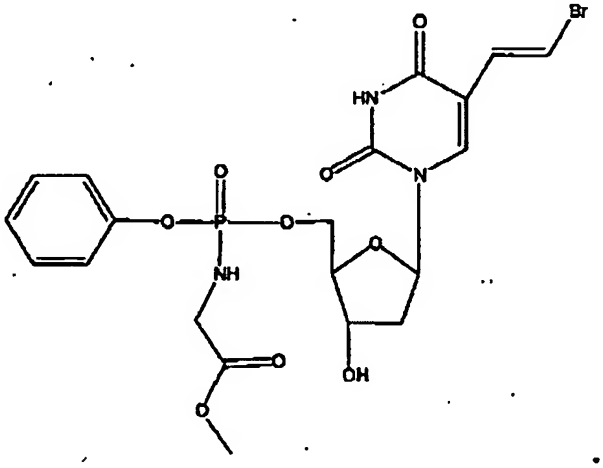
20. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



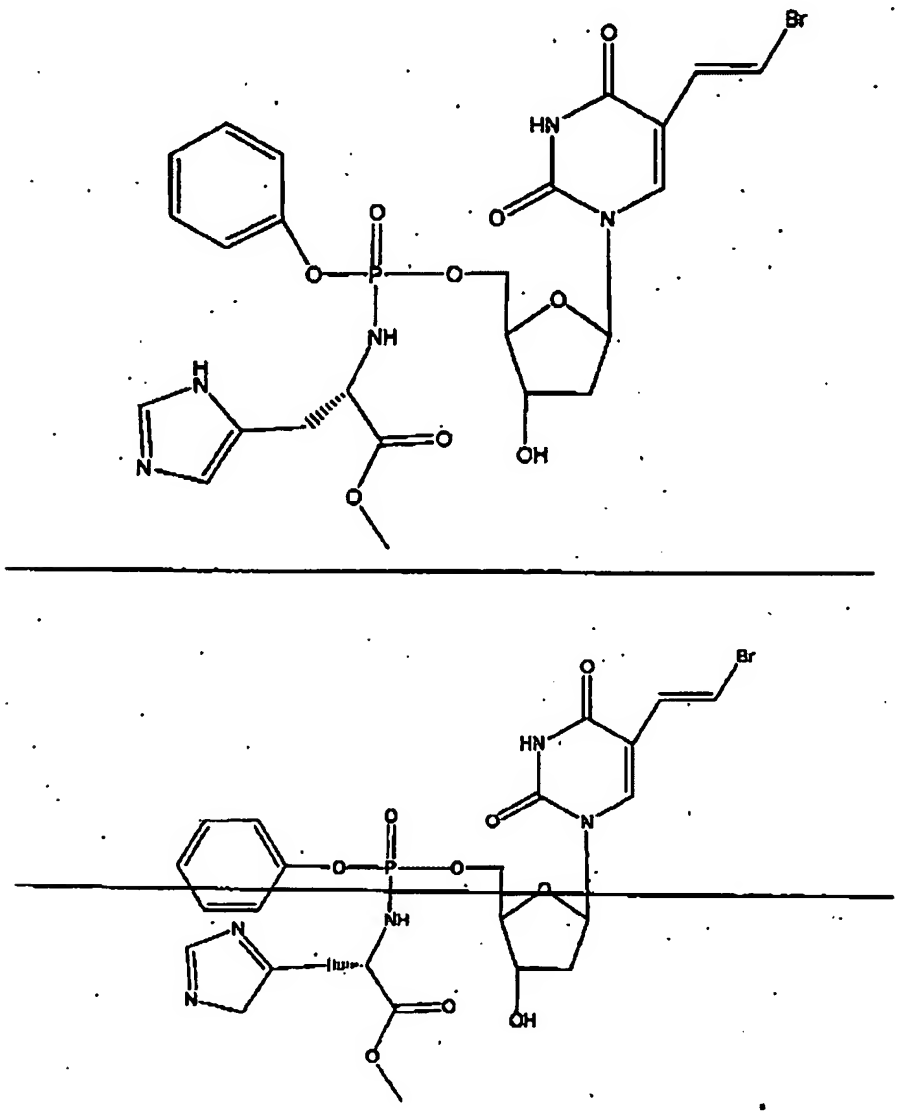
21. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



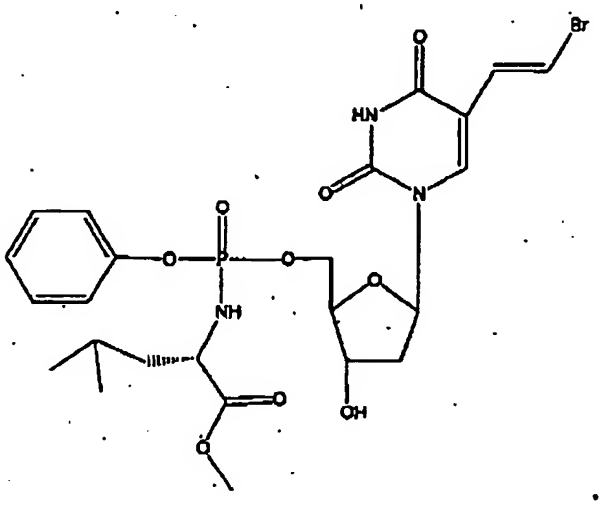
22. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



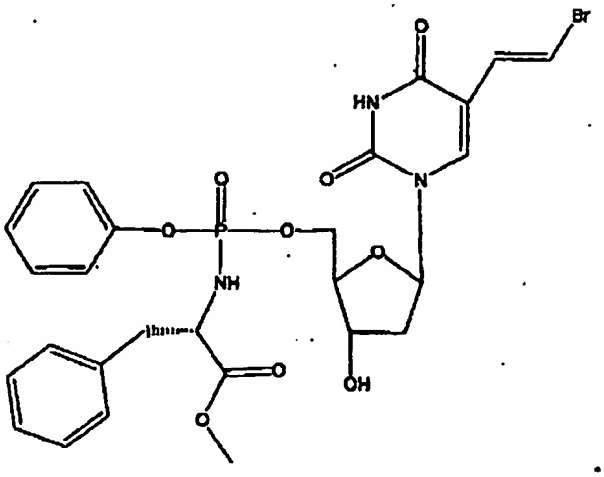
23. (Currently Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



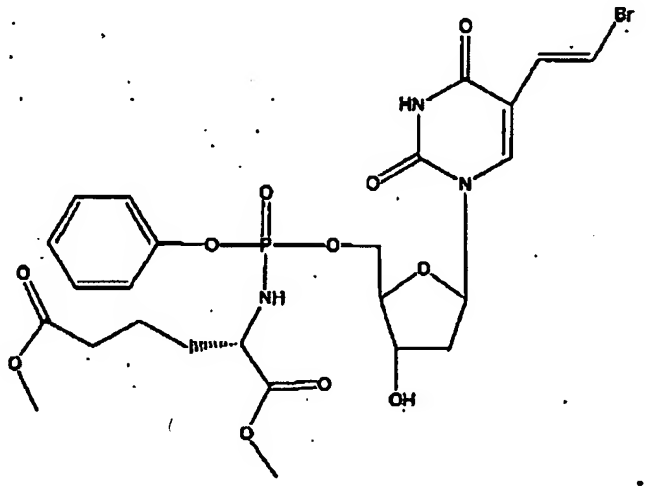
24. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



25. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



26. (Previously Amended) A compound or its pharmaceutically acceptable salt, ester or ether, wherein the compound has the formula:



27. (Original) A composition comprising the compound of claim 1 and a carrier.

28. (Original) A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier..

29. (Previously Amended) A method of inhibiting the proliferation of a cancer cell comprising contacting the cancer cell with an effective amount of the compound of claim 1 or a metabolite thereof.

30. (Previously Amended) A method for treating a cell or tissue related to an autoimmune disorder or an inflammatory condition, comprising contacting the cell or tissue with an effective amount of the compound of claim 1 or a metabolite thereof.

31. (Previously Added) The method of claim 29, wherein the cancer cell is a colon cancer cell or a breast cancer cell.

32. (Previously Added) The method of claims 29 or 30, wherein the contacting is *in vitro*.

33. (Previously Amended) The method of claims 29 or 30, wherein the contacting is *in vivo*.

34. (Withdrawn) The composition of claim 27, further comprising an effective amount of a nucleoside transport inhibitor.

35. (Withdrawn) The method of claim 29, further comprising administering an effective amount of a nucleoside transport inhibitor.

36. (Withdrawn) The method of claim 29, wherein the treatment comprises reversing resistance to a chemotherapeutic.

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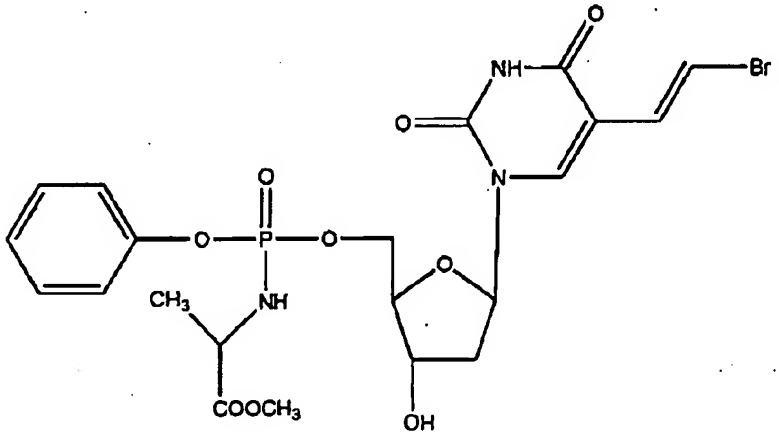
I. AMENDMENTS AND LISTING OF CLAIMS

Listing of Claims

The following listing of the claims supersedes and replaces all prior amendments and claim listings.

1. (Currently Amended) A method for treating a subject having ~~an autoimmune disorder or inflammatory condition~~ rheumatoid arthritis comprising delivering to the subject an effective amount of an L- or D- compound of the formula:



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or its 5' monophosphate derivative, and wherein the compound or its 5' monophosphate derivative may be in any of its enantiomeric, disasteriomeric, stereoisomeric or anomeric forms ~~of a compound the selected from the group consisting of a 1,5- substituted pyrimidine derivative or analog and a substituted furano-pyrimidone derivative or analog~~.

2. (Withdrawn) The method of claim 1, wherein the compound is a 1,5-substituted deoxyuridine derivative or analog.

3. (Withdrawn) The method of claim 1, wherein the compound is a substituted furanopyrimidone derivative or analog.

4. (Canceled)

5. (Withdrawn) The method of claim 2, wherein the 1,5-substituted deoxyuridine is substituted at the 5 position with a substituent selected from the group consisting of alkyl, alkenyl, alkynyl, vinyl, propargyl and substituted derivatives thereof.

6. (Withdrawn) The method of claim 5, wherein the substituted derivatives are halogen-substituted derivatives.

7. (Withdrawn) The method of claim 6, wherein the halogen-substituted derivative is a 5-haloalkyl substituted deoxyuridine.

8. (Withdrawn) The method of claim 7, wherein the compound is 5-bromovinyl substituted deoxyuridine.

9. (Withdrawn) The method of claim 4, wherein the 1,5-substituted deoxyuridine is a 5'-phosphoryl derivative of pyrimidine.

10. Claims 10 to 13 (Canceled)

11. (Withdrawn) The method of claim 1, wherein the subject has an inflammatory condition.

12. (Withdrawn) The method of claim 14, wherein the inflammatory condition is selected from the group consisting of psoriasis, ulcerative colitis, scleroderma, inflammatory bowel disease, asthma, and Crohn's disease.

13. (Withdrawn) The method of claim 1, further comprising administering an effective amount of an agent that treats an autoimmune and/or inflammatory condition.

14. (Withdrawn) The method of claim 16, wherein the agent is selected from the group consisting of a corticosteroid, a N-SAID, an anti-rheumatic drug and an anti-TNF agent.

15. (Withdrawn) A method for treating cells or tissue involved in a pathology selected from the group consisting of an autoimmune disease and an inflammatory condition, comprising contacting the cells or tissue with an effective amount of a compound selected from the group consisting of a 1,5- substituted pyrimidine derivative or analog and a substituted furano-pyrimidone derivative or analog thereof.

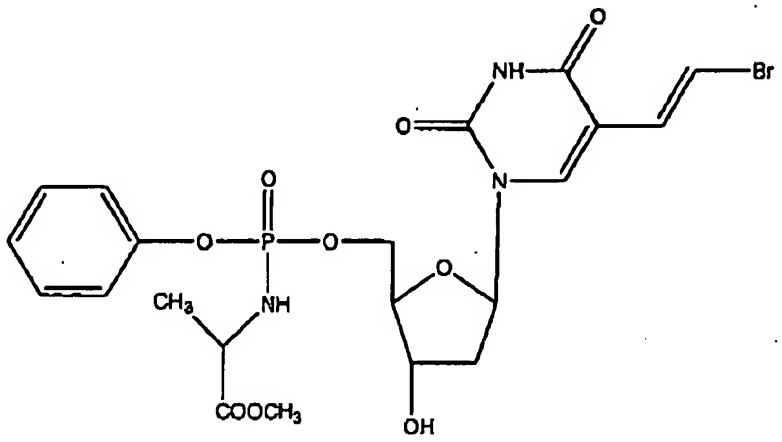
16. (Withdrawn) The method of claim 18, wherein the compound is (*E*)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

17. (Withdrawn) An assay for selecting agents that treat cells or tissue involved in a pathology selected from the group consisting of an autoimmune disease and an inflammatory condition, comprising contacting a first sample comprising suitable cells or tissue with an effective amount of a compound selected from the group consisting of a deoxyuridine, a substituted deoxyuridine, a substituted deoxyuridine derivative and analogs thereof and contacting a second sample of the suitable cells or tissue with the agent to be assayed and comparing the treatment of the first and second samples.

18. (Withdrawn) The assay of claim 20, further comprising contacting the agent with a third sample of cells or tissue comprising normal counterpart cells or tissue to the second sample and selecting agents that treat the second sample of cells or tissue but does not adversely effect the third sample.

19. (Withdrawn) The assay of claim 21, wherein the substituted deoxyuridine derivative is (*E*)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

20. (New) The method of claim 1, wherein the compound is an L- or D- compound of the formula:



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and wherein the compound may be in any of its enantiomeric, disasteriomeric, sterioisomeric or anomeric forms.